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Spotlight on Research Advances

This issue of the FYI from the NHLBI highlights several recent NHLBI-supported scientific advances.

Genomic Mapping Finds Multiple Genes Related to Heart Disease Risk Factors

Scanning the genomes of more than 100,000 people from all over the world, scientists reported the largest set of genes yet discovered that underlie blood lipid variations known to be major risk factors for coronary heart disease.

A research team from 17 countries found 95 genetic variants—arrangements of the nucleic acids in DNA that differ among people—that contribute to changes in blood cholesterol and triglyceride levels in men and women of many ethnic backgrounds. Taken together, the gene variants explain between one-quarter and one-third of the inherited portions of cholesterol and triglyceride measured in the blood. Of the variants, 59 had not been identified and thus provide new clues for developing effective medicines to combat heart disease.

This exciting discovery follows upon similar research, reported last year, regarding another heart disease risk factor—hypertension. Using genomic analysis of over 29,000 participants from the Framingham Heart Study and other cohorts, an international research team identified a number of unsuspected genetic variants associated with systolic and diastolic blood pressure. Although hypertension has long been known to run in families and have a substantial genetic component, previous attempts to identify genes associated with blood pressure had met with only limited success.

The new findings from both the lipid and the blood pressure studies illustrate the potential of large-scale genome-wide association studies to identify genes that play a role in a complex disease of widespread public health importance.

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12th Annual PIO Meeting is in the Planning Stages

The 12th Annual NHLBI Public Interest Organization Meeting is scheduled to be held on May 23rd and 24th, 2011, in Bethesda, MD. The program will feature topical scientific presentations, timely discussions, and a setting that encourages attendees to interact and share experiences and ideas.

Please help our planning efforts by ensuring that the NHLBI has the most up-to-date contact information for your organization. If there have been any changes in leadership, mailing addresses, email addresses, or phone numbers for your PIO, please contact us at NHLBIPIOMeeting@nhlbi.nih.gov.

Inside

Upcoming NHLBI Workshops and Working Groups*

No activities are scheduled for the period covering January through April 2011.

Research Advances

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Exercise and Nutrition Interventions Improve Blood Pressure

The DASH diet—an eating plan low in saturated and total fat and high in fruits, vegetables, and fat-free or low-fat dairy products—had been shown to reduce blood pressure (BP) among participants in short-term "feeding" studies, but its efficacy in lowering BP had not been demonstrated in real-world settings. The Exercise and Nutrition Interventions for Cardiovascular Health (ENCORE) study was a community trial in overweight, sedentary adults with above-normal BP who were assigned to follow the DASH diet, either alone or combined with a behavioral weight-management program that included supervised exercise, or to continue their usual eating patterns.

By itself the DASH diet yielded a systolic BP decrease of 8 mm Hg, and when it was combined with weight management a decrease of 12 mm Hg was achieved in comparison with continuation of usual behavior. The magnitude of BP change achieved in ENCORE was similar to that obtained with a high dose of a single antihypertensive medication.

BP reductions of this magnitude in placebo-controlled treatment trials have resulted in a 40-percent reduction in stroke risk and a 25-percent reduction in ischemic heart disease risk.

Genetic Studies Yield Progress Toward Prediction of Aortic Aneurysms

Thoracic aortic aneurysm and dissection (TAAD)—enlarging and then tearing of the aorta—is often asymptomatic until a catastrophic cardiovascular event occurs. Prospective diagnosis of TAAD is challenging because no reliable biomarkers for it have yet been identified and many of its risk factors are unknown.

A genetic strategy to identify individuals at risk for TAAD could help prevent sudden deaths from this disease. Mutations in two genes that encode for proteins that regulate the contraction of aortic smooth muscle cells (SMCs) are known to cause familial forms of TAAD, suggesting that impairment of the ability of SMCs to contract may predispose to non-familial forms of TAAD.

To explore this hypothesis, investigators performed a genome-wide analysis of 418 patients with sporadic (non-familial) TAAD. They identified 47 copy number variants (CNVs)—regions of the genome that are deleted or duplicated—that appeared more frequently in patients with TAAD than in normal controls. Although no single CNV was strongly associated with TAAD, many of the CNVs within the set of 47 contain genes that are in some manner involved in contraction of SMCs.

These findings suggest that the genetic variants governing SMC function are a potential target for the development of predictive tests.

Sildenafil May Help Patients with Idiopathic Pulmonary Fibrosis (IPF)

Few treatments are available for patients with IPF, a rapidly fatal condition in which tissue deep in the lungs becomes thick and stiff, causing shortness of breath and severely limiting diffusion of oxygen into the bloodstream.

A randomized, placebo-controlled clinical trial undertaken by the IPF Clinical Research Network evaluated treatment with sildenafil (a drug known to relax blood vessels in the lungs and allow blood to flow more easily) versus placebo in 180 patients with advanced IPF.

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Mark Your Calendar . . .

February	American Heart Month *(www.americanheart.org)*
4th	National Wear Red Day *(www.nhlbi.nih.gov/health/heart-truth)*
7th-14th	Congenital Heart Defect Awareness Week *(www.tchin.org/aware)*
May	National High Blood Pressure Education Month *(www.nhlbi.nih.gov/about/nhbpep/)*

NHLBI Research Initiatives

From time to time, the NHLBI invites investigators to submit grant applications or contract proposals for specific research programs. We are soliciting applications for the following new programs. Please visit the URL listed with each program to obtain information about application dates and deadlines. For full descriptions of these and other current research initiatives, visit www.nhlbi.nih.gov/funding/inits/index.htm.

Translating Basic Behavioral and Social Science Discoveries into Interventions to Improve Health-Related Behaviors (R01) (PA-11-063)
http://grants.nih.gov/grants/guide/pa-files/PA-11-063.html
Objective: Encourage highly innovative research projects that propose to translate findings from basic research on human behavior into effective clinical, community, and population-based behavioral interventions.

Toward An Improved Understanding of HDL Function, NHLBI (R01) (PA-11-012)
http://grants.nih.gov/grants/guide/pa-files/PA-11-012.html
Objective: Develop, validate, and standardize assays to measure high density lipoprotein (HDL) function and biomarkers for HDL function and to identify novel genes, pathways, and potential therapeutic targets in relation to HDL function.

Sickle Cell Disease: Inflammation, Thrombosis, and Vascular Dysfunction (R01) (PA-11-013)
http://grants.nih.gov/grants/guide/pa-files/PA-11-013.html
Objective: Encourage research that will lead to a better understanding of the role of the immune and coagulation systems in the vaso-occlusive pathologies associated with sickle cell disease.

NIH Basic Behavioral and Social Science Opportunity Network (OppNet) Short-term Mentored Career Development Awards in the Basic Behavioral and Social Sciences for Mid-career and Senior Investigators (K18) (RFA-DE-11-003)
http://grants.nih.gov/grants/guide/rfa-files/RFA-DE-11-003.html
Objective: Support short-term mentored career development (K18) awards in the basic behavioral and social sciences research from three months to one year in duration.

NIH Basic Behavioral and Social Science Opportunity Network (OppNet) Short-term Interdisciplinary Research Education Program for New Investigators (R25) (RFA-NR-11-002)
http://grants.nih.gov/grants/guide/rfa-files/RFA-NR-11-002.html
Objective: Support short-term R25 Research Education Project applications that will focus on providing creative and innovative education research experiences for new scientists in basic behavioral and social science research.

NHLBI Translational Research Implementation Program (TRIP) - Limited Competition - (P50) (RFA-HL-12-003)
http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-12-003.html
Objective: Accelerate the translation of promising new therapeutic interventions derived from fundamental research discoveries for the treatment and prevention of cardiovascular, lung, and blood diseases.

Chronic Illness Self-Management in Children and Adolescents (R01) (PA-11-070 and PA-11-072)
http://grants.nih.gov/grants/guide/pa-files/PA-11-070.html
Objective: Encourage research to improve self-management and quality of life in children and adolescents with chronic illnesses.

Getting from Genes to Function in Lung Disease (R01) (PA-11-011)
http://grants.nih.gov/grants/guide/pa-files/PA-11-011.html
Objective: Identify and characterize the function of gene(s) and their associated variants involved in lung diseases by genome-wide association studies or other genetic approaches.

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Although 12 weeks of sildenafil treatment yielded no improvement in exercise capacity, sildenafil users experienced small but significant benefits with respect to arterial oxygenation, carbon monoxide diffusion capacity, shortness of breath, and quality of life.

The improvement in symptoms, in and of itself, could be very important to IPF patients, who currently have so few options. In addition, the significant physiological findings encourage researchers to continue to investigate this promising drug treatment.

First Recipient of Gene Therapy for Beta-Thalassemia Responds Well

Researchers have published a three-year progress report of the first-ever human gene therapy trial in a patient with beta-thalassemia, an inherited disorder of hemoglobin formation.

In June 2007 a retroviral vector was used to deliver therapeutic genes to an adult who suffered from severe thalassemia and had been dependent on monthly blood transfusions since childhood. For the past two years the patient has maintained near-normal hemoglobin levels and has not needed any transfusions. Moreover, no undesirable side effects have been observed.

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National Heart, Lung, and Blood Advisory Council Meetings

September 1, 2010

Dr. Susan B. Shurin, Acting Director of the NHLBI, welcomed members to the 239th meeting of the National Heart, Lung, and Blood Advisory Council (NHLBAC). The entire meeting, which Council members attended via video conference and telephone, was a closed session for the consideration of grant applications.

October 26, 2010

Dr. Shurin welcomed members to the 240th meeting of the NHLBAC. She recognized five Council members who are retiring: Ms. Jeanine Arden Ornt, Dr. Shaun Coughlin, Dr. Joe Garcia, Ms. Paula Polite, and Dr. Steven Shapiro.

Dr. Shurin welcomed representatives of three NHLBI Advisory Committees: Dr. C. William Balke, representing the NHLBI Institutional Training Mechanism Review Committee; Dr. Charles Czeisler, representing the Sleep Disorder Research Advisory Board; and Dr. Curt D. Sigmund, representing the Heart, Lung, and Blood Program Project Review Committee. Dr. Edward Benz, of the Sickle Cell Disease Advisory Committee, and Dr. Julio Panza of the Clinical Trials Review Committee were unable to attend.

Dr. Shurin noted several NIH-level issues:

A preliminary injunction issued on August 23, 2010, by the U.S. District Court for the District of Columbia halted the use of federal funds for human embryonic stem cell research. As of October 25, 2010, NIH-supported stem cell research was allowed to continue pending appeal.

The NIH Scientific Management Review Board Sub-Working Group on Substance Use, Abuse, and Addiction recommended creation of a new Addiction Institute wherein all relevant addiction research portfolios from the National Institute on Alcohol Abuse and Alcohol, the National Institute on Drug Abuse, and other Institutes/Centers would be integrated. The NIH Director has authority to accept or reject the recommendation.

The Cures Acceleration Network, part of the Patient Protection and Affordable Care Act, will seek to reduce the time it takes to develop new treatments and cures by reducing barriers between laboratory discoveries and clinical

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News from Capitol Hill

Appropriations for Fiscal Year (FY) 2011

The 2011 fiscal year (FY) began on October 1, 2010. Since September 30, 2010, the Congress has passed four temporary funding measures, called continuing resolutions (CR), to fund federal the government. The fourth CR, P.L. 111-322, which became law on December 22, 2010, funds most federal government programs, including the NIH, at FY 2010 levels through March 4, 2011. The new Congress, which began in January 2011, will need to pass additional measures to fund government programs after the continuing resolution ends on March 4.

House Passes the Acquired Bone Marrow Failure Disease Research and Treatment Act

On September 30, 2010, the House passed H.R. 1230, a bill introduced by Representative Doris Matsui (D-CA) to provide for research on acquired bone marrow failure diseases. The bill amends the Public Health Service Act to state that the DHHS Secretary may conduct research on acquired bone marrow failure diseases, including research on characteristics of affected individuals and genetic and environmental factors that may be associated with the diseases. On November 15, 2010, the bill was received in the Senate and referred to the Senate committee on Health, Education, Labor, and Pensions.

House Passes the Scleroderma Research and Awareness Act

On September 30, 2010, the House passed H.R. 2408, a bill introduced by Representative Lois Capps (D-CA) that would amend the Public Health Service Act to authorize the NIH Director to expand, intensify, and coordinate scleroderma activities at the NIH. On November 15, 2010, the bill was received in the Senate and referred to the Senate committee on Health, Education, Labor, and Pensions.

House Recognizes Sickle Cell Disease Awareness Month; Senate Commemorates 100th Anniversary of the First Description of Sickle Cell Anemia

On September 28, 2010, the House passed a resolution (H. Res. 1663), introduced by Representative Martha Fudge (D-OH), to recognize the goals and ideals of sickle cell disease awareness month, which is observed each September. On November 18, 2010, the Senate passed by unanimous consent a resolution (S. Res. 685) introduced by Senator Benjamin Cardin (D-MD) to commemorate the 100th anniversary of the 1910 description of sickle cell disease by Dr. James B. Herrick. The resolution highlights the NIH symposium held on November 16-17 to commemorate the 100th anniversary and recognizes the contribution of the biomedical research community to the improvement in diagnosis and treatment of sickle cell disease. The resolution also recognizes the National Heart, Lung, and Blood Institute for its role in reporting the first effective drug treatment for adults with severe sickle cell disease.

Upcoming Events

Activity	Date/Location	More Information
Parent Heart Watch 6th Annual National Conference	January 14 –16, 2011 San Diego, CA	http://www.parentheartwatch.org/ActionAdvocacy/Events.aspx
National Heart, Lung, and Blood Advisory Council 241st Meeting	February 15, 2011 Bethesda, MD	http://www.nhlbi.nih.gov/meetings/nhlbac/index.htm
National Sleep Foundation Sleep Health & Safety 2011	March 17 – 20, 2011 Washington, DC	http://www.sleepfoundation.org/events-activities
The LAM Foundation International Lymphangioleiomyomatosis Research Conference	April 8 – 10, 2011 Cincinnati, OH	http://www.thelamfoundation.org
Hemophilia Federation of America 2011 Symposium	April 14 – 16, 2011 Louisville, KY	http://hemophiliafed.org/programs-and-services/symposium/
Adult Congenital Heart Association Sixth National Conference	April 28 – May 1, 2011 Los Angeles, CA	http://www.achaheart.org/news/conferences.php
Alpha-1 Association 20th Annual National Education Conference	June 10 – 12, 2011 St. Paul, MN	http://www.alpha1.org/education/nateduconf.php
National Heart, Lung, and Blood Advisory Council 242nd Meeting	June 15, 2011 Bethesda, MD	http://www.nhlbi.nih.gov/meetings/nhlbac/index.htm
Tuberous Sclerosis Alliance 2011 International TSC Research Conference	July 6 – 9, 2011 Washington, DC	http://www.tsalliance.org/pages.aspx?content=564
Take Off Pounds Sensibly Club, Inc. International Recognition Days	July 7 – 9, 2011 Milwaukee, WI	http://www.tops.org/Events/IRD2011.aspx
Cardio-Facio-Cutaneous Syndrome International 6th International CFC Family Conference & Clinic Program	July 28 – 30, 2011 Rosemont, IL	http://www.cfcsyndrome.org/conference.shtml
Narcolepsy Network 25th Annual Patient Conference	October 13 – 15, 2011 Las Vegas, NV	http://www.narcolepsynetwork.org/news-and-events/conferences/

First Recipient of Gene Therapy for Beta-Thalassemia Responds Well

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Thalassemia affects millions of people worldwide and is responsible for considerable mortality, especially among children in developing countries, and significant use of health-care resources due to the need for chronic blood transfusions and therapies for the resulting iron overload. Heretofore the only strategy for correcting the hemoglobin defect has been bone marrow transplantation, a procedure not available to most patients.

Demonstration of long-term safety and efficacy of gene therapy in this patient and others would constitute a breakthrough that could substantially reduce the public health burden of thalassemia and improve the lives of those who suffer from it.

Constituents' Corner

No constituents' submissions were received for this issue.

We invite you to use this space that we reserve for you to share your successes and opinions. You may submit your ideas and articles to nhlbi.listens@nih.gov or Public Interest News, Office of Science and Technology, Building 31, Room 5A07, 31 Center Drive, MSC-2482, Bethesda, MD 20892-2482.

October 2010 Advisory Council Meeting

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trials. The FY 2011 President's Budget identifies $50 million for the Network.

The NIH has completed a therapeutics inventory to identify activities (including development of drugs, biologics, and devices) under way at the NIH, with the goal of accelerating translational medicine and advancing therapeutics development. The NHLBI is carefully considering where in the drug development pipeline to focus its investments.

The NIH will reconfigure its diversity programs (in light of recent legal decisions) to focus on populations defined as disadvantaged, rather than on race or ethnicity. Future Funding Opportunity Announcements will include revised NIH diversity language and state the compelling need that it will address. The NIH Diversity Task Force will assess workforce diversity at the NIH and make recommendations on diversification of the intramural and extramural workforce.

The Patient-Centered Outcomes Research Institute (PCORI), a non-profit non-governmental body authorized under the Patient Protection and Affordable Care Act, was established to help stakeholders make informed health decisions.

The NIH faces a number of challenges in the area of comparative effectiveness research (CER) including, for example, setting criteria for priorities, supporting next-generation CER, and helping researchers use observational data.

The NIH is currently operating under a Continuing Resolution, which means that the NHLBI must operate at its FY 2010 budget level of $3,095,812,000. Dr. Shurin reviewed the Institute's proposed FY 2011 President's Budget, noting that no substantial change in the distribution between funding mechanisms is anticipated for FY 2011.

Dr. Shurin noted that the NIH anticipates resubmission in FY 2011 of a substantial number of applications initially submitted for funding under the American Recovery and Reinvestment Act (ARRA), which will most likely exacerbate recent declines in the success rate. The NHLBI is planning carefully in order to preserve current levels of investigator-initiated awards.

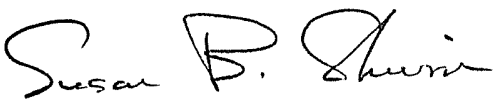
Dr. Carl Roth, Acting Deputy Director and Associate Director for Scientific Program Operation, NHLBI, presented an analysis of the Institute's differential payline policy, instituted in FY 2010, and submission data for FY 2010. He also presented results of an analysis of the revised scoring system and enhanced review criteria for competing NIH applications that were instituted beginning with the summer 2009 review cycle.

Dr. Andrew Arai, Chief of the Cardiovascular and Pulmonary Branch, Division of Intramural Research, NHLBI, and Dr. Peter Kellman, Staff Scientist at the Laboratory of Cardiac Energetics, Division of Intramural Research, NHLBI, discussed the NHLBI's bench-to-bedside research program in cardiovascular MRI, which includes technical developments in cardiovascular MRI, use of MRI in acute coronary syndrome, MRI-guided interventions and MRI-guided robot surgery, and diagnostic and interventional research in pediatrics and congenital heart disease.

NHLBI staff presented 10 new initiatives, 5 renewals, and 2 requests by other ICs for secondary support, all of which had been reviewed in September by the Board of External Experts. The Council was mostly supportive of the initiatives presented, but made a number of specific recommendations for consideration prior to their release.

Need More Information?

We are always interested in receiving comments and suggestions from the community. If you or your organization have questions for me or for the Institute, please contact me at shurinsb@nhlbi.nih.gov or Dr. Carl Roth at rothc@nhlbi.nih.gov.



Susan B. Shurin, M.D.
Acting Director, NHLBI

For information on specific issues, the following contacts may be helpful:

- For health-related questions, information about publications, or communications pertaining to NHLBI policies and priorities, please contact the trained information specialists of the NHLBI Information Center at 301-592-8573, or write to the Information Center at P.O. Box 30105, Bethesda, MD 20824-0105, or email inquiries to nhlbiinfo@nhlbi.nih.gov.
- For additional information regarding NHLBI events, consult the references provided or www.nhlbi.nih.gov/calendar/nhcal.htm. Most other NIH Institutes and Centers also maintain calendars on their Web sites. Links to their Web pages are at www.nih.gov/icd.